CLAIMS

1. A fusion protein comprising a heat shock protein fused to a single epitope-containing segment, the epitope-containing segment comprising two or more identical epitopes.

2. The fusion protein of Claim 1 wherein the heat shock protein is ubiquitin and the fusion protein is a ubiquitin fusion protein.

3. The ubiquitin fusion protein of Claim 2 wherein the epitope-containing segment is fused to ubiquitin at a fusion site selected from the group consisting of the N-terminus, the C-terminus and an internal fusion site.

4. The ubiquitin fusion protein of Claim 2 wherein the N-terminal residue of ubiquitin is a residue other than methionine, and the N-terminal residue other than methionine is fused to the C-terminal residue of a second, unmodified ubiquitin protein.

5. The ubiquitin fusion protein of Claim 2 wherein the N-terminal residue of ubiquitin is a residue other than methionine, and the N-terminal residue other than methionine is fused to the C-terminal residue of a C-terminal ubiquitin subdomain competent to specify cleavage by a ubiquitin-specific protease between the C-terminal residue of the C-terminal ubiquitin subdomain and the N-terminal residue other than methionine.

6. The ubiquitin fusion protein of Claim 5 wherein at least one epitope-containing segment is positioned between the C-terminal residue of the C-terminal

ubiquitin subdomain and the N-terminal residue other than methionine, and the C-terminus of the C-terminal subdomain is modified to inhibit cleavage by a ubiquitin-specific protease.

7. The ubiquitin fusion protein of Claim 2 which is post-translationally modified by the addition of fatty acids to enhance immunogenicity.

8. The ubiquitin fusion protein of Claim 2 wherein the epitope-containing segment contains from about 2 to about 30 epitopes.

9. The ubiquitin fusion protein of Claim 2 wherein the identical epitopes are B cell epitopes.

10. The ubiquitin fusion protein of Claim 2 wherein the identical epitopes are T cell epitopes.

11. The ubiquitin fusion protein of Claim 2 wherein the identical epitopes are structural mimics of biomolecules.

12. The ubiquitin fusion protein of Claim 2 wherein the identical epitopes are microbial epitopes.

13. The ubiquitin fusion protein of Claim 2 wherein the identical epitopes are self epitopes.

14. The ubiquitin fusion protein of Claim 2 wherein the identical epitopes represent epitopes from the proteins selected from the group consisting of gonadotropin releasing hormone, tumor necrosis factor, immunoglobulins, human immunodeficiency virus proteins,

chorionic gonadotrophin, inhibin, growth hormones and sperm proteins.

15. The ubiquitin fusion protein of Claim 2 wherein the identical epitopes which comprise the plurality of identical epitopes are gonadotropin releasing hormone epitopes.

16. The ubiquitin fusion protein of Claim 2 wherein internal fusion sites comprise regions of ubiquitin linking two domain of secondary structure, the two domains of secondary structure being selected from the group consisting β-strand and α-helix.

17. The ubiquitin fusion protein of Claim 2 wherein the epitope-containing segment is fused to the C-terminus of ubiquitin and the C-terminus of ubiquitin is modified to inhibit cleavage of the ubiquitin fusion protein by a ubiquitin-specific protease.

18. The ubiquitin fusion protein of Claim 17 wherein the C-terminus of ubiquitin is modified at amino acid 76.

19. The ubiquitin fusion protein of Claim 18 wherein the modification at amino acid 76 of ubiquitin is a substitution of an amino acid selected from the group consisting of: alanine, valine, and cysteine for the wild-type glycine amino acid residue.

20. A fusion protein comprising a heat shock protein fused to two or more non-contiguous epitope-containing segments, each epitope-containing segment comprising one or more identical or non-identical epitopes.

21. The fusion protein of Claim 20 wherein the heat shock protein is ubiquitin and the fusion protein is a ubiquitin fusion protein.

22. The ubiquitin fusion protein of Claim 21 wherein the non-contiguous epitope-containing segments are fused to ubiquitin at fusion sites selected from the group consisting of the N-terminus, the C-terminus and internal fusion sites.

23. The ubiquitin fusion protein of Claim 21 wherein the N-terminal residue of ubiquitin is a residue other than methionine, and the N-terminal residue other than methionine is fused to the C-terminal residue of a second, unmodified ubiquitin protein.

24. The ubiquitin fusion protein of Claim 21 wherein the N-terminal residue of ubiquitin is a residue other than methionine, and the N-terminal residue other than methionine is fused to the C-terminal residue of a C-terminal ubiquitin subdomain competent to specify cleavage by a ubiquitin-specific protease between the C-terminal residue of the C-terminal ubiquitin subdomain and the N-terminal residue other than methionine.

25. The ubiquitin fusion protein of Claim 24 wherein at least one epitope-containing segment is positioned between the C-terminal residue of the C-terminal ubiquitin subdomain and the N-terminal residue other than methionine, and the C-terminus of the C-terminal subdomain is modified to inhibit cleavage by a ubiquitin-specific protease.

26. The ubiquitin fusion protein of Claim 21 which is post-translationally modified by the addition of fatty acids to enhance immunogenicity.

27. The ubiquitin fusion protein of Claim 21 wherein the epitope-containing segments contain from about 1 to about 30 epitopes.

28. The ubiquitin fusion protein of Claim 21 wherein one epitope-containing segment contains at least one B cell epitope and one T cell epitope.

29. The ubiquitin fusion protein of Claim 21 wherein one epitope-containing segments contains at least two B cell epitopes.

30. The ubiquitin fusion protein of Claim 21 wherein one epitope-containing segments contains at least two T cell epitopes.

31. The ubiquitin fusion protein of Claim 21 wherein one or more epitopes contained within the epitope-containing segments are structural mimics of biomolecules.

32. The ubiquitin fusion protein of Claim 21 wherein one or more epitopes contained within the epitope-containing segments are microbial epitopes.

33. The ubiquitin fusion protein of Claim 21 wherein one or more epitopes contained within the epitope-containing segments are self epitopes.

34. The ubiquitin fusion protein of Claim 21 wherein one or more epitopes contained within the epitope-containing segments represent epitopes from the group of proteins

selected from the group consisting of gonadotropin releasing hormone, tumor necrosis factor, immunoglobulins, human immunodeficiency proteins, chorionic gonadotrophin, inhibin, growth hormones and sperm proteins.

35. The ubiquitin fusion protein of Claim 21 wherein one or more epitopes contained within the epitope-containing segments represent epitopes from gonadotropin releasing hormone.

36. The ubiquitin fusion protein of Claim 21 wherein the internal fusion sites comprise regions of ubiquitin linking two domain of secondary structure, the two domains of secondary structure being selected from the group consisting β-strand and α-helix.

37. The ubiquitin fusion protein of Claim 21 wherein one epitope-containing segment comprises a single B-cell epitope or a plurality of identical or non-identical B-cell epitopes and a second epitope-containing segment comprises a single T-cell epitope or a plurality of identical or non-identical T-cell epitopes.

38. The ubiquitin fusion protein of Claim 21 wherein at least one epitope-containing segment is fused to the C-terminus of ubiquitin and the C-terminus of ubiquitin is modified to inhibit cleavage of the ubiquitin fusion protein by a ubiquitin-specific protease.

39. The ubiquitin fusion protein of Claim 38 wherein the C-terminus of ubiquitin is modified at amino acid 76.

40. The ubiquitin fusion protein of Claim 21 wherein the modification at amino acid 76 of ubiquitin is a

substitution of an amino acid selected from the group consisting of: alanine, valine, and cysteine for the wild-type glycine amino acid residue.

41. A fusion protein comprising a heat shock protein fused to a single epitope-containing segment comprising two or more identical or non-identical epitopes, the epitope-containing segments being fused to the heat shock protein at fusion sites selected from the group consisting of the N-terminus and an internal fusion site.

42. The fusion protein of Claim 41 wherein the heat shock protein is ubiquitin and the fusion protein is a ubiquitin fusion protein.

43. The ubiquitin fusion protein of Claim 42 wherein single epitope-containing segment contains from about 2 to about 30 identical or non-identical epitopes.

44. The ubiquitin fusion protein of Claim 42 wherein the N-terminal residue of ubiquitin is a residue other than methionine, and the N-terminal residue other than methionine is fused to the C-terminal residue of a second, unmodified ubiquitin protein.

45. The ubiquitin fusion protein of Claim 42 wherein the N-terminal residue of ubiquitin is a residue other than methionine, and the N-terminal residue other than methionine is fused to the C-terminal residue of a C-terminal ubiquitin subdomain competent to specify cleavage by a ubiquitin-specific protease between the C-terminal residue of the C-terminal ubiquitin subdomain and the N-terminal residue other than methionine.

46. The ubiquitin fusion protein of Claim 45 wherein at least one epitope-containing segment is positioned between the C-terminal residue of the C-terminal ubiquitin subdomain and the N-terminal residue other than methionine, and the C-terminus of the C-terminal subdomain is modified to inhibit cleavage by a ubiquitin-specific protease.

47. The ubiquitin fusion protein of Claim 42 which is post-translationally modified by the addition of fatty acids to enhance immunogenicity.

48. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains at least one B cell and one T cell epitope.

49. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains at least two B cell epitopes.

50. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains at least two T cell epitopes.

51. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains epitopes which are structural mimics of biomolecules.

52. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains epitopes which are microbial epitopes.

53. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains epitopes which are self epitopes.

54. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains at least one epitope from proteins selected from the group consisting of gonadotrophin releasing hormone, tumor necrosis factor, immunoglobulins, human immunodeficiency virus proteins, chorionic gonadotrophin, inhibin, growth hormones and sperm proteins.

55. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains epitopes from gonadotropin releasing hormone.

56. The ubiquitin fusion protein of Claim 42 wherein the internal fusion site comprises a region of ubiquitin linking two regions of secondary structure selected from the group consisting of β-strand and α-helix.

57. The ubiquitin fusion protein of Claim 42 wherein the epitope-containing segment contains a single B-cell epitope or a plurality of identical or non-identical B-cell epitopes and a second epitope-containing segment comprises a single T-cell epitope or a plurality of identical or non-identical T-cell epitopes.

58. A fusion protein comprising a heat shock protein fused to a single epitope-containing segment comprising one or more identical or non-identical epitopes, the epitope-containing segment being fused to the heat shock protein at the N-terminus of the heat shock protein.

59. The fusion protein of Claim 58 wherein the heat shock protein is ubiquitin and the fusion protein is a ubiquitin fusion protein.

60. The ubiquitin fusion protein of Claim 59 wherein the epitope-containing segment contains from about 1 to about 30 epitopes.

61. The ubiquitin fusion protein of Claim 59 wherein the N-terminal residue of ubiquitin is a residue other than methionine, and the N-terminal residue other than methionine is fused to the C-terminal residue of a second, unmodified ubiquitin protein.

62. The ubiquitin fusion protein of Claim 59 wherein the N-terminal residue of ubiquitin is a residue other than methionine, and the N-terminal residue other than methionine is fused to the C-terminal residue of a C-terminal ubiquitin subdomain competent to specify cleavage by a ubiquitin-specific protease between the C-terminal residue of the C-terminal ubiquitin subdomain and the N-terminal residue other than methionine.

63. The ubiquitin fusion protein of Claim 62 wherein at least one epitope-containing segment is positioned between the C-terminal residue of the C-terminal ubiquitin subdomain and the N-terminal residue other than methionine, and the C-terminus of the C-terminal subdomain is modified to inhibit cleavage by a ubiquitin-specific protease.

64. The ubiquitin fusion protein of Claim 59 which is post-translationally modified by the addition of fatty acids to enhance immunogenicity.

65. The ubiquitin fusion protein of Claim 59 wherein the epitope-containing segment contains at least one B cell epitope and one T cell epitope.

66. The ubiquitin fusion protein of Claim 59 wherein the epitope-containing segment contains at least two B cell epitopes.

67. The ubiquitin fusion protein of Claim 59 wherein the epitope-containing segment contains at least two T cell epitopes.

68. The ubiquitin fusion protein of Claim 59 wherein one or more epitopes contained within the epitope-containing segment is a structural mimic of a biomolecule.

69. The ubiquitin fusion protein of Claim 59 wherein one or more epitopes contained within the epitope-containing segment is a microbial epitope.

70. The ubiquitin fusion protein of Claim 59 wherein one or more epitopes contained within the epitope-containing segment is a self epitope.

71. The ubiquitin fusion protein of Claim 59 wherein one or more epitopes contained within the epitope-containing segment represents an epitope from the group of proteins selected from the group consisting of gonadotropin releasing hormone, tumor necrosis factor, immunoglobulins, human immunodeficiency proteins, chorionic gonadotrophin, inhibin, growth hormones and sperm proteins.

72. The ubiquitin fusion protein of Claim 59 wherein one or more epitopes contained within the epitope-containing segment represents an epitope from gonadotropin releasing hormone.

73. The ubiquitin fusion protein of Claim 59 wherein the epitope-containing segment contains a single B-cell epitope or a plurality of identical or non-identical B-cell epitopes and a second epitope-containing segment comprises a single T-cell epitope or a plurality of identical or non-identical T-cell epitopes.

74. A DNA construct encoding a fusion protein of Claims 20, 41, or 58.

75. A cell containing a DNA construct encoding a fusion protein of Claims 1, 20, 41 or 58.

76. A method for stimulating an immune response in an animal, the immune response being directed toward a ubiquitin fusion protein, the method comprising:
a) providing a ubiquitin fusion protein comprising ubiquitin fused to a single epitope-containing segment, the epitope-containing segment comprising two or more identical epitopes; and
b) administering the fusion protein of step a) to an animal under conditions appropriate for the stimulation of an immune response.

77. A method for stimulating an immune response in an animal, the immune response being directed toward a ubiquitin fusion protein, the method comprising:
(a) providing a ubiquitin fusion protein comprising ubiquitin fused to two or more non-contiguous epitope-containing segments, each epitope-containing segment comprising one or more identical or non-identical epitopes; and
(b) administering the fusion protein of step a) to an animal under conditions appropriate for the stimulation of an immune response.

78. A method for stimulating an immune response in an animal, the immune response being directed toward a ubiquitin fusion protein, the method comprising:
(a) providing a ubiquitin fusion protein comprising ubiquitin fused to a single epitope-containing segment comprising two or more identical or non-identical epitopes, the epitope-containing segments being fused to ubiquitin at fusion sites selected from the group consisting of the N-terminus and an internal fusion site;
(b) administering the fusion protein of step a) to an animal under conditions appropriate for the stimulation of an immune response.

79. A method for stimulating an immune response in an animal, the immune response being directed toward a ubiquitin fusion protein, the method comprising:
(a) providing a ubiquitin fusion protein comprising ubiquitin fused to a single epitope-containing segment comprising one or more identical or non-identical epitopes, the epitope-containing segment being fused to ubiquitin at N-terminus of ubiquitin;
(b) administering the fusion protein of step a) to an animal under conditions appropriate for the stimulation of an immune response.

80. A method for stimulating an immune response in an animal, the immune response being directed toward a fusion protein, the method comprising:
a) providing a DNA construct encoding a fusion protein of Claims 1, 20, 41 or 58;
b) introducing the DNA construct of step a) into the cells of the animal under conditions appropriate for expression.

81. A ubiquitin fusion protein comprising ubiquitin having the peptide QHWSYGLRPGQHWSYGLRPGQHWSYGLRPGQHWSYGLRPGC fused via its N terminus to the C-terminal residue of ubiquitin, the ubiquitin fusion protein being cleavable by a ubiquitin-specific protease.

82. The fusion protein of Claim 81 conjugated to an immunogenic carrier protein.

83. A ubiquitin fusion protein comprising ubiquitin having the peptide QHWSYGLRPGQHWSYGLRPGQHWSYGLRPGQHWSYGLRPG fused via its N terminus to the C-terminal residue of ubiquitin, the ubiquitin moiety being modified such that the ubiquitin fusion protein is non-cleavable by a ubiquitin-specific protease.

84. A method for stimulating an immune response in an animal, the immune response being directed toward a ubiquitin fusion protein, the method comprising:
(a) providing a ubiquitin fusion protein comprising ubiquitin having the peptide QHWSYGLRPGQHWSYGLRPGQHWSYGLRPGQHWSYGLRPGC fused via its N terminus to the C-terminal residue of ubiquitin; and
(b) administering the conjugate of step (a) to an animal under conditions appropriate for the stimulation of an immune response.

85. The method of Claim 84 wherein the physiological consequences of administration to the animal are substantially similar to the consequences of surgical castration.

86. A method for the identification of antibodies in experimental or diagnostic samples, comprising:

a) providing a ubiquitin fusion protein of selected from the group consisting of ubiquint fusion proteins described in Claims 1, 20, 41 and 58;
b) providing antibodies from an experimental or clinical source;
c) forming an incubation mixture comprising the ubiquitin fusion protein of step a) and the antibodies of step b); and
d) detecting binding of the antibodies of step b) to the ubiquitin fusion protein of step a).

87. A method for reducing levels of a predetermined protein in an animal relative to base-line levels, comprising:
a) providing a ubiquitin fusion protein of selected from the group consisting of ubiquitin fusion proteins described in Claims 1, 20, 41 and 58 which contain at least one epitope representing an epitope from the predetermined protein and
b) administering the fusion protein of step a) to the animal under conditions appropriate for the stimulation of an immune response.

88. The method of Claim 87 wherein the predetermined protein is a peptide hormone.

89. The method of Claim 88 wherein the predetermined peptide hormone is a male-specific or female-specific peptide hormone.

90. The method of Claim 89 wherein the predetermined peptide hormone is gonadotropin releasing hormone.

91. The method of Claim 87 wherein the predetermined protein is tumor necrosis factor.

92. The method of Claim 87 wherein the predetermined protein is a growth hormone protein.

93. The method of Claim 87 wherein the fusion protein is conjugated to a non-ubiquitin carrier protein.

94. A method for reducing levels of a predetermined protein in an animal relative to base-line levels, comprising:
    a) providing a DNA construct encoding a ubiquitin fusion protein of selected from the group consisting of ubiquitin fusion proteins described in Claims 1, 20, 41 and 58 which contain at least one epitope representing an epitope from the predetermined protein; and
    b) introducing the DNA construct of step a) into the cells of an animal under conditions appropriate for the expression and stimulation of an immune response.

95. The method of Claim 94 wherein the predetermined protein is a peptide hormone.

96. The method of Claim 95 wherein the predetermined peptide hormone is a male-specific or female-specific peptide hormone.

97. The method of Claim 96 wherein the predetermined peptide hormone is gonadotropin releasing hormone.

98. The method of Claim 94 wherein the predetermined protein is tumor necrosis factor.

99. The method of Claim 94 wherein the predetermined protein is a growth hormone protein.

100. The method of Claim 94 wherein the fusion protein is conjugated to a non-ubiquitin carrier protein.